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DISPLACEMENT OF PLASMA PROTEIN AND CONDUCTION VELOCITY IN RATS
UNDER ACTION OF ACCELERATION FORCES AND HYPOKINESIA

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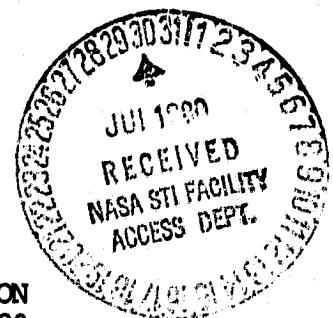
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16. Abstract In animals undergoing action of +5Gz accelerations, no increase in vascular permeability, as tested with the use of ⁵¹ Cr-globulin, was demonstrated. In rats immobilized for 4 weeks before centrifugation rather weak migration of ⁵¹ Cr-globulin from the vessels was observed. Immobilization resulted also in lowering of conduction velocity in the sciatic nerve.			
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Introduction

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In previous studies [1] it was established that an acceleration of +5Gz operating during a period of from 15 min to 3 hrs induces changes based on the displacement of ¹³¹I-albumins in accordance with the direction of the accelerating action. It was also shown that the observed changes were dependent on the migration of proteins from the blood vessels. In later studies [2, 3] attention was directed to homodynamic [sic] disturbances occurring in animals affected by acceleration following a prolonged period of hypokinesia.

The survival rate of animals subjected to acceleration after prolonged hypokinesia declined and such animals could not stand the stress of centrifugation for longer than a period of 37 min. Moreover, it was found that there was a significantly more marked migration of I-albumin through the blood vessels under the influence of longitudinal acceleration. This change was accompanied by disturbances of a functional nature within the peripheral neuron together with the motor cell of the anterior horn /62 of the spinal chord. Changes of this kind may be dangerous for the organism under conditions of high altitude and space flights. A useful result of these points of view has been research conducted in the area of the permeability of the capillary vessels. Authors carried out tests to find out, whether it was acceleration alone or acceleration following prolonged hypokinesia which induced the occurrence of changes leading to penetration of the vascular walls by I-albumins exclusively or also proteins with larger molecules, i. e. globulin.

Method

The experiment was conducted on 70 white Wistar rats weighing about 200-250 g.

* Numbers in the margin indicate pagination in the foreign text.

The animals were divided into 2 groups: experiment and control. The experimental group comprised 40 animals kept during 4 weeks under conditions of complete immobility by being placed in special immobility cages that prevented any movement (Fig. 1).

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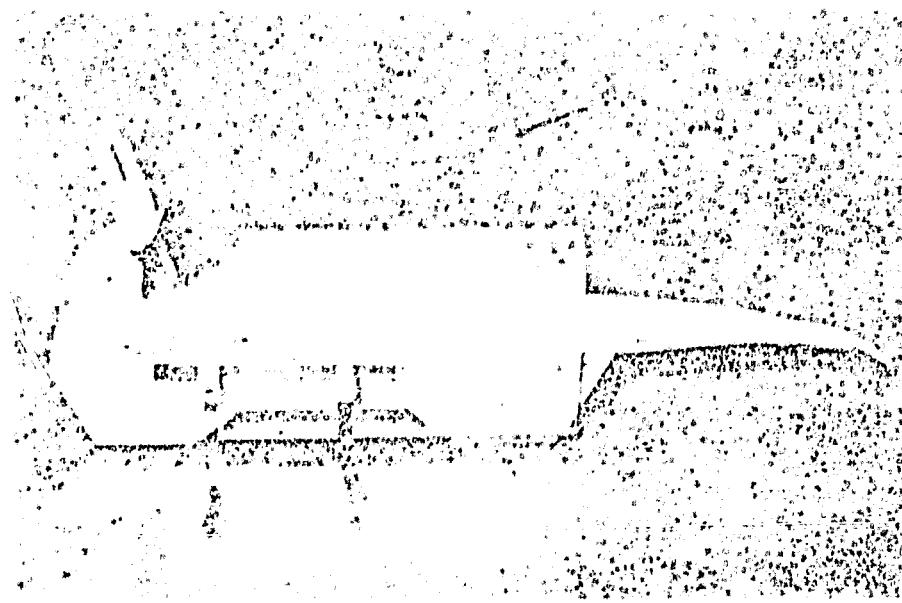


Fig. 1. Rat in cage restricting mobility.

Feeding was done by means of specially adapted containers. Following 4 weeks /63 of immobilization the animals of this group were subjected to an acceleration of +5Gz during periods of 15 min, 1 hr, 2 hrs and 3 hrs. Each of these subgroups numbered 10 animals. The control group was represented by 30 animals. This control group was subjected to acceleration only for 15 min, 1 hr and 2 hrs. During the entire experiment the animals in this group were maintained under normal vivarium conditions.

A special centrifuge (Fig. 2) was used for carrying out the experiment. It was adapted for experimental tests on animals, making it possible to centrifuge 4 rats simultaneously.

The animals were placed in special receptacles in such a way that the vector of centrifugal force traversed the long body axis in a craniocaudal direction. Before centrifuging was begun the animals of both groups, i. e. experimental and control, received intravenously ⁵¹Cr-globulin in the amount of 100 units per gram body weight.

At the end of the designated time rotation was stopped, the animals subjected to /64 ether anesthesia, and dehematized, whereupon segments of the muscles of the forelimbs and hindlimbs were taken to measure radioactivity using the method presented in previous works [1, 2, 3]. Radioactivity of the selected samples was determined in amounts of imp/min/mg of dry tissue. A percentage calculation was made of the difference in radioactivity between the muscles of the forelimbs and the hindlimbs, taking the former as 100%. In several cases, both for the control and experimental groups, a scintigram was taken.

For measuring conduction velocity we used the method proposed by Hodes et al. [4]. At two points along the course of the anatomic sciatic nerve we placed 2 stimulating needle electrodes: adducent and educent. They were placed 1 cm apart and connected with a DISA stimulator (Multistim) with a transformer as an insulation unit. The stimulating electrode used was a concentrating needle electrode of the type DISA 13K 04, length 42 mm and cross section 0.65 mm. The muscular potential produced was recorded from the gastrocnemius muscle using the educent concentrating electrode DISA 13K 51. Supramaximal stimuli were used, that exceeded maximal stimuli by 20 volts. Stimuli frequency was one cycle per second. Recording was done on a three channel electromyogram DISA with an input impedance of 200 megaohms.

Conduction velocity measurement was done on a group of 40 animals subjected to examination just before immobilization and at the end of the 4 week immobilization cycle. No assessment was made of the effect of centrifugation on conduction velocity.

Test Results and Evaluation

Table I shows the difference in radioactivity of the muscles of the forelimbs and hindlimbs for both control and centrifuged animals following prolonged immobilization.

From the data presented above we see that in the case of the control animals, /65 i. e. those kept in normal vivarium conditions, and then subjected to acceleration for 15 min, 1 hr and 2 hrs, there was no occurrence of extravascular proteins labeled with chromium and consequently ⁵¹Cr-globulin. For this reason experiments with this group were abandoned following 3 hrs of acceleration. On the other hand in the experimental group the presence of Cr-globulins was not noted extravascularly

TABLE I. RADIOACTIVITY CHANGES IN ^{51}Cr -GLOBULIN IN MUSCLES OF CONTROL RATS AND GROUP COMPLETELY IMMOBILIZED FOR 28 DAYS, FOLLOWING HYPOKINESIA

Acceleration time	Con-trol	Animals after immobilization	Diff-erence
15 min	99,8	98,9	- 0,9
1 godz	100,5	101,2	+ 0,7
2 godz	100,9	111,4	+ 10,5
3 godz	-	113,4	-

TABLE II. EFFECT OF 8 WEEK IMMOBILIZATION OF RATS UPON CONDUCTION VELOCITY IN THE SCIATIC NERVE

	Mean standard deviation, $\bar{X} \pm S$	Significance of difference
Before immobilization	$54,2 \pm 3,17$	p 0,001
After 8 weeks of immobilization	$48,83 \pm 2,03$	

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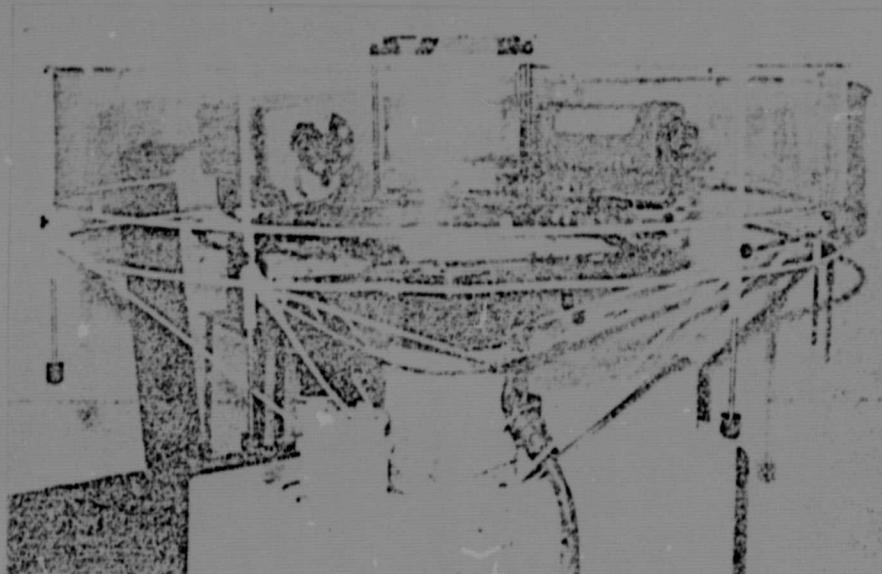


Fig. 2. Centrifuge for studying the effect of acceleration on small laboratory animals.

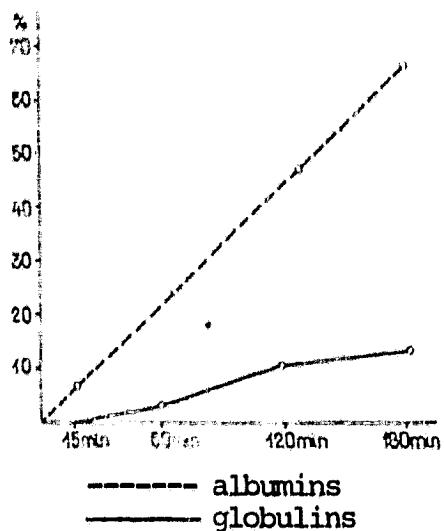


Fig. 3. Migration of ^{131}I -albumin and ^{51}Cr -globulin from the vessels of animals centrifuged after 4 weeks of immobilization.

in line with the effect of experiment time. The tests above permit us to estimate that 1 month of hypokinesia has only an insignificant effect on hemodynamic changes in the organism during the time of acceleration.

Restricted mobility increases permeability of the vessels under the influence /66 of acceleration not only for micromolecular proteins but also for macromolecular proteins, such as the globulins, which in a very insignificant degree may penetrate beyond the vessels. The scintigrams produced no new data. They did not show any place where the red coloring was evidence of much penetration of ^{51}Cr -globulin beyond the vascular bed.

In testing the penetration of albumins by the use of ^{131}I -albumin it was shown that in ratio to the time increase in acceleration there is increased escape of such proteins from the vascular bed amounting to 64% after 3 hrs. These results, in our opinion, are evidence of significant hemodynamic disturbances in peripheral circulation. However, determination of the migration of ^{51}Cr -globulin through the vascular walls indicates only an insignificant amount of permeability for these proteins. Even after 2-3 hrs of centrifugation the differences ranged from 5 to 10% /67 and were therefore significantly lower than for ^{131}I -albumin. The works of Czerski et al. [5, 6], using the Keti tests, likewise showed increased permeability of the

following 15 min or 1 hr of acceleration at +5 Gz. However, the data obtained after 2 and 3 hours of centrifugation support the hypothesis, that ^{51}Cr -globulins find their way out of the vascular bed only to an insignificant degree. The graph in Fig. 3 illustrates the dynamics of such changes.

This graph likewise shows the penetration of the wall by ^{131}I -labeled protein and therefore ^{131}I -albumin [2]. In the course of these curves there is a considerable difference in permeability of the vascular wall for proteins of different molecular size. Previous studies [1, 2, 3] made it possible to assert that these changes regress in a rather significant degree

vessels for ^{22}Na even when acceleration was in the range of +3 G and continued for several hours. These authors, using multiple acceleration over a long period of time, even demonstrated the presence of histopathological changes in the walls of blood vessels. These changes were characterized by distention of the cells that gave the impression of transudate changes. Similar changes were observed by Senelar et al. [7] in experiments on dogs subjected to the protracted effect of acceleration of +2.5 Gz. From the above data we may judge, that the time period of hypokinesia used in our experiments did not produce irreversible changes in the vessels themselves as well as in their muscular bed. On the other hand, the dissimilarity between the present results and those of previous studies [1, 2, 3] as well as the studies of the authors cited [5, 6] is in all likelihood based on the size of the molecules penetrating the vascular walls. In our experiments we tested this kind of penetrability for large molecules and single acceleration. It is possible that multiple acceleration, even under the conditions of our experiments, might produce the same changes noted by other authors. In the present experiment we did not use the method of multiple acceleration because we wished to have our experimental conditions approximate reality as closely as possible. An astronaut who finds himself in conditions of limited mobility and reduced gravitation is subjected to the effect of acceleration once and for a relatively short time. The same is true on plane flights where the pilot is not exposed for a long time to acceleration.

An analysis of conduction velocity measurements in the sciatic nerve of rats subjected to compelled immobility showed a statistically reliable reduction in velocity in respect to the above values. Numerical data are presented in Table II.

It appears that the observed reduction in the velocity of impulse conduction was occasioned by changed conditions in the blood supply to the nerve fibers and the associated disturbances of a metabolic nature. Skorpil [8] called attention to the fact/68 that reduced motor activity may induce changes in conduction velocity. However, the very strong views of this author in regard to this kind of effect are based upon highly myelinated fibers and therefore on greater conduction velocity.

Final Conclusions

As a result of the experiments conducted it was shown:

1. Subjecting the animals to acceleration in the amount of +5 Gz for 15 min to 2 hrs did not induce penetration of the vascular wall by macromolecular proteins such as globulins.
2. Keeping animals for a long time under conditions of immobility does little to favor penetrability of the vessels by macromolecular proteins. Permeability for ^{51}Cr -globulin is considerably less than for ^{131}I -albumin.
3. Immobilization of the animals for 4 hours induces a statistically significant reduction in the conduction velocity of the sciatic nerve.

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